

WHAT IS CLAIMED IS:

1. A method for controlling the operation of a digital-type microfluidic (“MF”) device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:
- 10 (a) providing one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either
- (i) creating one or more new micro-droplets at selected stable positions, or
- (ii) moving one or more micro-droplets from current stable positions to
- 15 selected next stable positions, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
- (iv) mixing one or more micro-droplets, and
- (b) generating control signals, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each
- 20 micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device.
- 25 2. The method of claim 1 wherein the control signals comprise electrical and optical signals.
3. The method of claim 1 wherein the MF device further comprises external control signals responsive to sensors internal to the MF device, and wherein the step of generating control
- 30 signals further comprises:
- (a) sensing control signals responsive to one or more internal MF device sensors; and
- (b) adjusting the generated signals that are provided to the MF device in response to the sensed signals so that the performance of a micro-droplet command
- 35 can be monitored.

4. The method of claim 1 wherein the step of creating a new micro-droplet further comprises separating the new micro-droplet from a fluid aliquot in a metered fashion .
5. The method of claim 1 wherein the step of creating a new micro-droplet further
5 comprises separating the micro-droplets from a source of fluid loaded into the MF device in a metered fashion .
6. The method of claim 1 wherein the step of moving a micro-droplet further comprises applying a force on the micro-droplet active to move the micro-droplet from the current
10 stable position to the next selected stable position.
7. The method of claim 6 wherein the step of applying a force further comprises generating a gas pressure acting on the micro-droplet.
- 15 8. The method of claim 1 wherein the step for combining two or more micro-droplets further comprises moving the micro-droplets into adjacency at the selected stable position.
9. The method of claim 1 wherein the step of mixing a micro-droplet further comprises moving the micro-droplet with sufficient speed to result in mixing.
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10. The method of claim 1 wherein each provided micro-droplet processing request further comprises one or more actuator processing requests,
wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device,
25 wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and
wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device
30 to function together to perform the requested action.
11. The method of claim 10 wherein the actuator processing requests comprise:
- (i) opening or closing a selected controlled passage by internal components acting as a controllable valve,
35 (ii) providing controllable gas pressure in a selected passage by internal components acting as pressure generator,

- (iii) sensing the presence or absence of a micro-droplets at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor, or
- 5 (iv) sensing the composition of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor.

12. The method of claim 11 wherein the step of opening or closing a controlled passage further comprises melting at least one aliquot of a meltable material, wherein the aliquot of the material is positionable for occluding the controlled passage.

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13. The method of claim 11 wherein the step of providing a gas pressure in a passage further comprises heating at least on gas micro reservoir communicating with the passage.

14. The method of claim 11 wherein the step of sensing the presence of a micro-droplet at a position in a passage further comprises sensing an indicator of the thermal capacity in a region about the position.

15. The method of claim 11 wherein the step of sensing the composition of a micro-droplet further comprises sending optical signals to the MF device and receiving optical signals returned from the MF device.

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16. The method of claim 11 wherein request for creating a new micro-droplet from a fluid aliquot in a passage further comprises:

- (i) one or more actuator processing requests to close the passage in order to prevent the fluid aliquot from moving in a reverse direction along the passage, and
- 25 (ii) one or more actuator processing requests to provide controllable gas pressure in order to pinch a new micro-droplet from the fluid aliquot in a metered manner and to propel the new micro-droplet to in a forward direction to the selected position.

30 17. The method of claim 11 wherein request for moving one or more new micro-droplets in a passage further comprises:

- (i) one or more actuator processing requests to close the passage in order to prevent the fluid aliquot from moving in a reverse direction along the passage, and
- (ii) one or more actuator processing requests to provide controllable gas pressure in order to propel the micro-droplet to in a forward direction to the next stable position.

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18. The method of claim 1 further comprising:

- 5 (a) before the step of providing a micro-droplet processing request, providing a micro-droplet processing program, wherein a micro-droplet processing program comprises one or more micro-droplet processing requests, and wherein the step of providing a micro-droplet processing request further comprises selecting an indicated request from the provided program, and
- (b) repeating the steps of providing a request and generating signals with each micro-droplet processing request until the provided program indicates that no further requests are available for selection.

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19. The method of claim 18 wherein the micro-droplet processing program comprises micro-droplet processing requests (i) for creating at least one initial micro-droplet from at least one fluid source, and (ii) for creating at least one final micro-droplet from the initial micro-droplets.

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20. The method of claim 17 further comprising, after the step of creating one or more additional micro-droplets, a step of detecting contents of certain of the additional micro-droplets.

20 21. The method of claim 1 wherein the internal components comprise heaters for applying spatially and temporally localized heating to the MF device, and wherein the control signals comprise electrical signals for activating the localized heaters.

22. The method of claim 21 wherein the internal components comprise at least one aliquot
25 of a meltable material arranged interior to a passage, and wherein the aliquot of material is associated with a heater for melting the material.

23. The method of claim 21 wherein the internal components comprise at least one gas micro reservoir, and wherein the gas micro reservoir is associated with a heater for heating
30 the gas to generate an increased pressure.

24. The method of claim 21 wherein the internal components comprise at least one temperature sensor that sense a local temperature of the MF device, and wherein the control signals include signals generated by the temperature sensor.

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25. The method of claim 21 wherein at least one temperature sensor is associated with a heater for sensing the sensing localized heating of the MF device by the heater.

26. A method for controlling the operation of a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:
- 10 (a) providing one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either
- (i) creating one or more new micro-droplets at selected stable positions, or
- 15 (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
- (iv) mixing one or more micro-droplets,
- 20 wherein each provided micro-droplet processing request further comprises one or more actuator processing requests,
- wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device, and wherein the actuator processing requests comprise,
- 25 (i) opening or closing a selected controlled passage by internal components acting as a controllable valve by melting at least one aliquot of a meltable material, wherein the aliquot of the material is positionable for occluding the controlled passage,
- (ii) providing controllable gas pressure in a selected passage by internal components acting as pressure generator by heating at least on gas micro
- 30 reservoir communicating with the passage
- (iii) sensing the presence or absence of a micro-droplets at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor by sensing an indicator of the thermal capacity in a
- 35 region about the position, or

(iv) sensing the composition of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor by sending optical signals to the MF device and receiving optical signals returned from the MF device, and

5 (b) generating control signals, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device,

10 wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and

15 wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device to function together to perform the requested action.

27. A method for controlling the operation of a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-
20 droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:

25 (a) providing one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either

(i) creating one or more new micro-droplets at selected stable positions by separating the new micro-droplet from an existing micro-droplet or a fluid source in a metered fashion, or

30 (ii) moving one or more micro-droplets from current stable positions to selected next stable positions by applying a gas pressure on the micro-droplet active to move the micro-droplet from the current stable position to the next selected stable position, or

35 (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions by moving the micro-droplets into adjacency at the selected stable position, or

(iv) mixing one or more micro-droplets by generating control signals for moving the micro-droplet with sufficient speed to result in laminar mixing, wherein each provided micro-droplet processing request further comprises one or more actuator processing requests,

5 wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device, and wherein the actuator processing requests comprise,

(i) opening or closing a selected controlled passage by internal components acting as a controllable valve,

10 (ii) providing controllable gas pressure in a selected passage by internal components acting as pressure generator,

(iii) sensing the presence or absence of a micro-droplets at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor, or

15 (iv) sensing the composition of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor, and

(b) generating control signals, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device,

20 wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and

25 wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device to function together to perform the requested action.

30 28. A method for performing a chemical reaction in a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:

- 5 (a) providing one or more fluid reagents, wherein the fluid reagents comprise the reactants necessary for the reaction,
- (b) creating at least one final micro-droplet from the fluid reagents by providing control signals to the MF device, wherein the micro-droplet is positioned at a stable position and comprises the reactants necessary for the reaction, and
- (c) reacting the micro-droplet.

10 29. The method of claim 28 wherein the step of reacting further comprises waiting for a time sufficient for occurrence of the reaction.

30. The method of claim 28 wherein the step of reacting further comprises exciting the final micro-droplet by providing control signals to the MF device, wherein the excitation is sufficient to cause occurrence of the reaction.

15 31. The method of claim 30 wherein the step of exciting comprises thermally heating or optically irradiating the micro-droplet.

32. The method of claim 28 further comprising a step of sensing the composition of the reacted micro-droplet by providing control signals to the MF device.

20 33. The method of claim 28 wherein the chemical reaction comprises performing the analysis of a sample.

34. The method of claim 28 wherein the step of creating further comprises:

- 25 (a) providing a micro-droplet processing request, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either
- (i) creating one or more new micro-droplets at selected stable positions, or
- 30 (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
- (iv) mixing one or more micro-droplets, and
- 35 (b) generating control signals for each micro-droplet processing request, which are provided to the MF device, wherein the control signals are generated in a pattern

and sequence that is responsive to each micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device.

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35. The method of claim 34 further comprising:

- 10 (a) before the step of providing a micro-droplet processing request, providing a micro-droplet processing program, wherein a micro-droplet processing program comprises one or more micro-droplet processing requests, and wherein the step of providing a micro-droplet processing request further comprises selecting an indicated request from the provided program, and
- (b) repeating the steps of providing a request and generating signals with each micro-droplet processing request until the provided program indicates that no further requests are available for selection.

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36. The method of claim 34 wherein each provided micro-droplet processing request further comprises one or more actuator processing requests,

wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device,

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wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and

wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device

25 to function together to perform the requested action.

37. The method of claim 36 wherein the actuator processing requests comprise:

- (i) opening or closing a selected controlled passage by internal components acting as a controllable valve,
- 30 (ii) providing controllable gas pressure in a selected passage by internal components acting as pressure generator,
- (iii) sensing the presence or absence of a micro-droplets at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor, or
- 35 (iv) sensing the composition of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor.

38. A method for performing a chemical reaction in a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and
5 (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:

- (a) providing one or more fluid reagents, wherein the fluid reagents comprise the reactants necessary for the reaction,
- 10 (b) providing a micro-droplet processing program, wherein a micro-droplet processing program comprises one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, and the requests comprising either
 - (i) creating one or more new micro-droplets at selected stable positions,
 - 15 or
 - (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or
 - (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
 - 20 (iv) mixing one or more micro-droplets,wherein the micro-droplet processing program provides for the creation of at least one final micro-droplet from the fluid reagents by providing control signals to the MF device, and wherein the micro-droplet is positioned at a stable position and comprises the reactants necessary for the reaction,
- 25 (c) selecting an indicated micro-droplet processing request from the provided processing program.
- (d) generating control signals for the selected micro-droplet processing request, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each micro-droplet processing request so
30 that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device,
- (e) repeating the steps of providing a request and generating signals with each micro-droplet processing request until the provided program indicates that no further
35 requests are available for selection, and

(f) reacting the micro-droplet by waiting for a time sufficient for occurrence of the reaction or by exciting the final micro-droplet by providing control signals to the MF device, wherein the excitation is sufficient to cause occurrence of the reaction.

5 39. A data acquisition ("DAQ")) system for controlling the operation of a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control
10 and monitoring the MF device, the system comprising:

(a) programmable digital control circuitry, wherein the digital control circuitry provides control signals to an MF device that is interfaced to the digital control circuitry, and

(b) memory accessible to the programmable digital control circuitry comprising
15 stored instructions and data representing one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either

(i) creating one or more new micro-droplets at selected stable positions,
or

20 (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or

(iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or

(iv) mixing one or more micro-droplets,

25 wherein execution of the instructions and data causes the programmable control circuitry to generate control signals in a pattern and sequence so that the responsive internal components of an interfaced MF device function together to perform the micro-droplet processing requests in the MF device.

30 40. The system of claim 39 further comprising at least one receptacle for receiving an interfaced MF device, wherein the receptacle provides for transfer of control signals between the programmable circuitry and an interface MF device.

41. The system of claim 39 wherein the programmable digital control circuitry further
35 comprises an interface to a host computer system, wherein a host computer system is accessible to a user for monitoring and controlling the operation of the DAQ system.

42. The system of claim 39 wherein the programmable digital control circuitry further comprises:

- (a) a processor, and
- (b) peripheral circuitry controllable by the processor for generating signals to an interfaced MF device.

43. The system of claim 42 wherein the peripheral circuitry further comprises:

- (a) driver circuitry for providing electrical control signals to an interfaced MF device, and
- (b) sensor circuitry for receiving electrical control signals from an interfaced MF device.

44. The system of claim 42 wherein the peripheral circuitry further comprises:

- (a) driver circuitry for providing optical control signals to an interfaced MF device, and
- (b) sensor circuitry for receiving optical control signals from an interfaced MF device.

45. The system of claim 39 wherein the instructions and data stored in the memory further comprise:

- (a) request data representing one or more micro-droplet processing requests, and
- (b) request-processing instructions, wherein execution of the request-processing instruction causes the programmable digital control circuitry to generate control signals for performing the represented micro-droplet processing requests in the MF device.

46. The system of claim 45 wherein the instructions and data stored in the memory further comprise:

- (a) micro-droplet configuration data representing identification of the micro-droplets present in an interfaced MF device and their respective positions,
- (b) device configuration data representing the state of internal components of an interfaced MF device, and
- (c) configuration-update instructions that cause update of the configuration data upon completion of a processing request.

47. The system of claim 46 wherein the request-processing instructions further comprise instructions to verify that a micro-droplet processing request is consistent with the micro-droplets configuration data.

- 5 48 The method of claim 45 wherein the instructions and data stored in the memory further comprise MF device structure data that represents the internal components of an interfaced MF device and their mutual arrangement.

49. A data acquisition ("DAQ")) system for controlling the operation of a digital-type
10 microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the system comprising:

- 15 (a) programmable digital control circuitry, wherein the digital control circuitry provides control signals to an MF device that is interfaced to the digital control circuitry, and
- (b) memory accessible to the programmable digital control circuitry comprising stored instructions and data representing
- 20 (I) actuator processing requests, wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device, the actuator requests comprising
- (i) opening or closing a selected controlled passage by internal components acting as a controllable valve,
- 25 (ii) providing controllable gas pressure in a selected passage by internal components acting as pressure generator,
- (iii) sensing the presence or absence of a micro-droplets at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor, or
- 30 (iv) sensing the composition of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor, and
- (II) one or more micro-droplet processing requests, wherein micro-droplet processing requests further comprise one or more actuator processing
- 35 requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either

- (i) creating one or more new micro-droplets at selected stable positions, or
- (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
- (iv) mixing one or more micro-droplets,

wherein execution of the instructions and data causes the programmable control circuitry to generate control signals in a pattern and sequence so that the responsive internal components of an interfaced MF device function together to perform a micro-droplet processing request in the MF device, and

wherein the generated pattern and sequence of control signals further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request. the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request causing the responsive internal components of the MF device to function together to perform the requested action.

50. The system of claim 49 wherein the programmable digital control circuitry further comprises:

- (a) a processor, and
- (b) peripheral circuitry controllable by the processor for generating signals to an interfaced MF device.

51. The system of claim 49 wherein the instructions and data stored in the memory further comprise:

- (a) MF-device-structure data that represents the internal components of an interfaced MF device and their mutual arrangement,
- (b) MF-device-configuration data representing the state of internal components of an interfaced MF device,
- (c) micro-droplet-configuration data representing identification of the micro-droplets present in an interfaced MF device and their respective positions,
- (d) request data representing one or more micro-droplet processing requests, wherein the micro-droplets are specified by reference to the micro-droplet-configuration data,

- (e) micro-droplet-processing-request data representing one or more actuator processing requests, wherein the actuators are specified by reference to the MF-device-structure data, and
- (f) request-processing instructions, wherein execution of the request-processing instruction causes the programmable digital control circuitry
- (i) to verify that a micro-droplet processing request is consistent with the micro-droplet-configuration data,
 - (ii) to verify that an actuator processing request is consistent with the MF-device-configuration data,
 - (iii) to generate control signals for performing the micro-droplet and actuator processing requests represented by the request data, and
 - (iv) to update the micro-droplet-configuration and the MF-device-configuration data upon completion of each processing request.

52. A computer readable medium comprising encoded instructions for causing a data acquisition system to perform the method of claim 1.

53. A computer readable medium comprising encoded instructions for causing a data acquisition system to perform the method of claim 26.